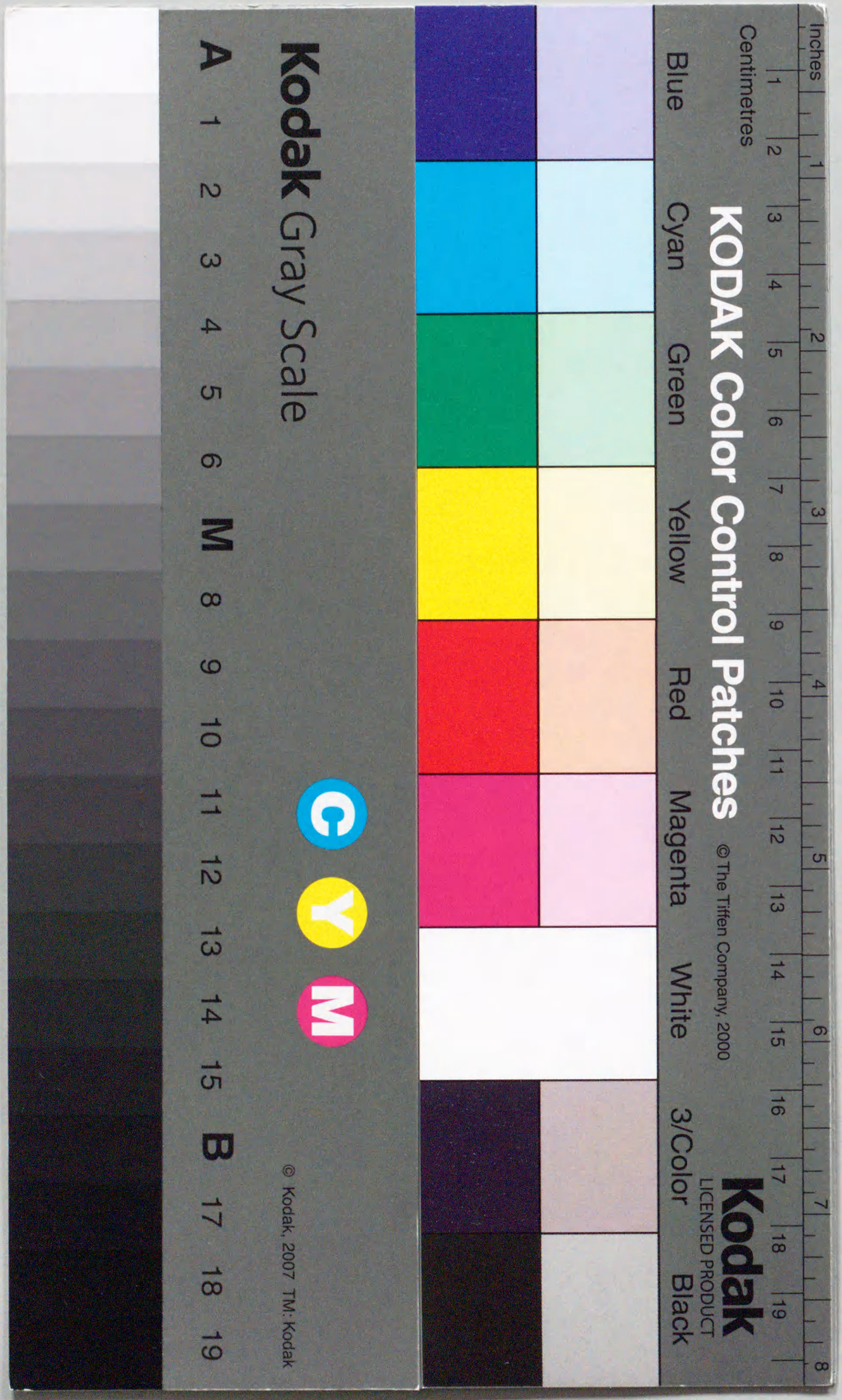

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Changes in Auditory Brainstem Responses of Normal Neonates Immediately after Birth

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Abstract. To clarify the functional changes in the acoustic conduction pathway in the human immediately after birth, auditory brainstem responses (ABR) in 58 normal neonates were examined. In longitudinal and cross-sectional analysis, the peak latency of wave 1 showed significant shortening ($p < 0.05$) from 1.82 ± 0.23 ms (mean ± SD) at 30 min after birth to 1.69 ± 0.26 ms at 2 h after birth. It continued to decrease gradually therafter. The interpeak latency of waves 1–3 decreased gradually (not significant) from 2.82 ± 0.19 ms (30 min after birth) to 2.74 ± 0.15 ms (1 month after birth), while the interpeak latency of waves 3–5 decreased significantly from 2.63 ± 0.27 ms (30 min after birth) to 2.47 ± 0.23 ms (24 h after birth; $p < 0.01$). These results indicate that functional changes in the acoustic system immediately after birth represent rapid adaptation of the peripheral region to the extrauterine environment and development of the more central region.

Introduction

Since Jewett et al. [1] reported the feasibility of auditory brainstem response (ABR) recording from the scalp, ABR has been clinically used for various purposes including auditory function testing in neonates and infants [2, 3], the assessment of maturity of the subcortical central nervous system in neonates and adults [4–6] and as an auxiliary diagnostic tool for neurological diseases. Recently, it has also begun to be used for brainstem function assessment in premature and mature neonates [7–9]. However, the adaptation of the human acoustic system to the sudden change in auditory enviroment after birth and the influence of stress during delivery on the neonatal acoustic system have not been sufficiently clarified [10]. In the past reports of ABR in normal human neonates, the times of ABR determination are not clear [2, 3, 8, 11–14] except in the report by

Rubinstein and Sohmer [15]. Even in the study by Rubinstein and Sohmer [15], who attempted to clarify the adaptation of the acoustic system to the extrauterine environment, ABR testing was not performed immediately after birth. Because of this, we recently followed the transition in the latencies of each ABR wave, starting 30 min after birth in the delivery room and taking into consideration the ABR-modifying factors (stress during delivery and properties of auditory stimuli) to assess the neonatal brainstem function.

Materials and Methods

Subjects wer 58 full-term neonates following an uneventful pregnancy without any maternal or fetal abnormalities. Five were delivered by scheduled cesarean section. Informed consent was obtained from the parents before delivery as to performing the ABR test on their children after birth. The duration of pregnancy ranged from 37 weeks 3 days to 40 weeks 2 days (mean: 38 weeks 3 days). Birth weight ranged from 2,652 to 3,506 g (mean ± SD: 3,158 ± 256). Each Apgar score was 8 or more at both 1 and 5 min after birth. An analysis of umbilical arterial blood revealed pH greater than 7.25, base excess greater than –10.0 mEq/l, P_{CO_2} less than 60 mm Hg and maximum total bilirubin less than 15 mg/dl. When examined 1 month after birth, all neonates showed normal growth and development.

ABR testing was performed on eight occasions: 0.5, 2, 4, 8 and 24 h and 2, 4 and 30 days after birth. The time of recording was strictly adhered to for the 5 recordings within 24 h after birth. Subsequent measurements were conducted during sleep after feeding. ABR testing was performed in a sound- and electricity-shielded area of the delivery room. During the ABR test 0.5 h after birth, the infant was kept warm with an infant warmer while monitoring rectal temperature to prevent hypothermia. Amniotic fluid remaining in the external acoustic meatus was carefully removed with a cotton wick. Subsequent ABR testings were performed on a cotton wick in the same room.

The instrument used for this study was a Neuropack 8 (Nihon Kohden) combined with a specially designed headphone for neonates. Two reference electrodes (one each on the bilateral mastoid processes) and one active electrode on the parietal region were fixed using dish electrodes and grounded to the frontal region. A stimulus sound (80 dB HL, 0.1 ms, 20-Hz click) was generated 2,048 times using a 200- to 3,000-Hz filter. ABR were recorded by an X-Y plotter and simultaneously stored in a microcomputer. Responses within 10.0 ms after stimulation were analyzed. On each occasion, the experiment was done in duplicate, and records in which all three waves 1, 3 and 5 were identified reproducibly were selected for evaluation. In the analysis of the ABR waves, the peak latency of wave 1, which represented peripheral conduction time, and the interpeak latencies of waves 1–3, 3–5 and 1–5, which represented central conduction time, were calculated. Student's t test and one-way analysis of variance (Anova) were used for statistical evaluation of intergroup differences in mean values and variances of these latencies.

Results

Table 1 shows the number of tests on each occasion. Records in which the peaks of waves 1, 3 and 5 were identifiable were obtained in 333 (93%) of 357 ABR tests. The percentage of good recordings was as high as 98% for ABR tests during sleep after feedings on the second and subsequent days. Records from 24 ABR tests could not be analyzed. The neonates were crying intensely and moving actively during most of those 24 ABR tests. The figures in parentheses in table 1 indicate the numbers of neonates delivered by scheduled cesarean section.

Longitudinal Analyses of ABR

Figure 1 shows the transition of the ABR from 30 min to 1 month after birth for a neonate delivered vaginally after 40 weeks and 2 days of gestation. In this neonate, peaks in waves 1, 3 and 5 were identified at each recording. Compared to the record obtained 30 min after birth, the peak latency for wave 1 showed a sharp decrease at 2 h, while those of the other two waves (3 and 5) decreased gradually until 8 or 24 h. Thereafter, the peak latency of each wave increased slightly on the second day, followed by a gradual decrease until 1 month after birth.

Figure 2 shows the transition of the peak latency of wave 1, and the interpeak latencies of waves 1–3 and 3–5, from 0.5 to 24 h after birth in 15 neonates in whom 5 ABR tests could be performed during this period. In 14 of 15 neonates the peak latency of wave 1 sharply decreased during the period from 0.5 to 2 h after birth. It then decreased gradually in most neonates. The interpeak latencies of waves 1–3 and 3–5 decreased in 11 and increased in 4 neonates during the first 2 h. Thereafter, they were varied, although the latency of waves 3–5 seemed to decrease until 4 h. Interindividual variances in these interpeak latencies were also larger than that in the peak latency of wave 1. There was no difference between vaginally delivered neonates and those delivered by scheduled cesarean section.

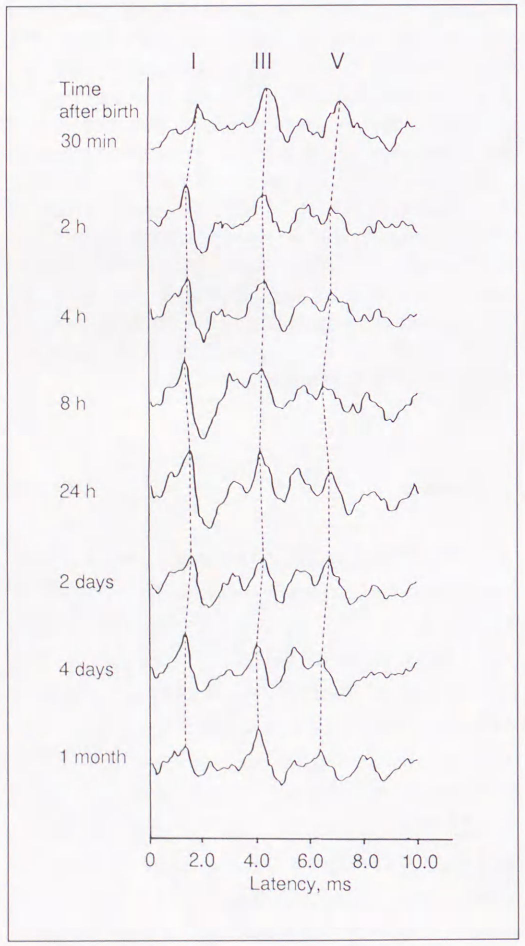

Fig. 1. Time course of ABR from 30 min to 1 month after birth in a neonate born at 40 weeks and 2 days of gestation. The peak latency of wave 1 (I) decreased sharply from 0.5 to 2 h, while the peak latencies of waves 3 and 5 (III and V) decreased gradually from 8 to 24 h after birth. Thereafter, all latencies increased slightly 2 days after birth, followed by a gradual decrease until 1 month after birth.

Table 1. Number and performance of ABR measurements on each occasion

Time after birth	Examinations n	Recording conditions good	Recording conditions bad
30 min	42 (5)	37 (5)	5
2 h	46 (5)	40 (5)	6
4 h	45 (5)	43 (5)	2
8 h	44 (5)	40 (5)	4
24 h	46 (5)	42 (5)	4
2 days	44	44	0
4 days	45	44	1
1 month	45	43	2

Neonates delivered by scheduled cesarean section are indicated in parentheses.

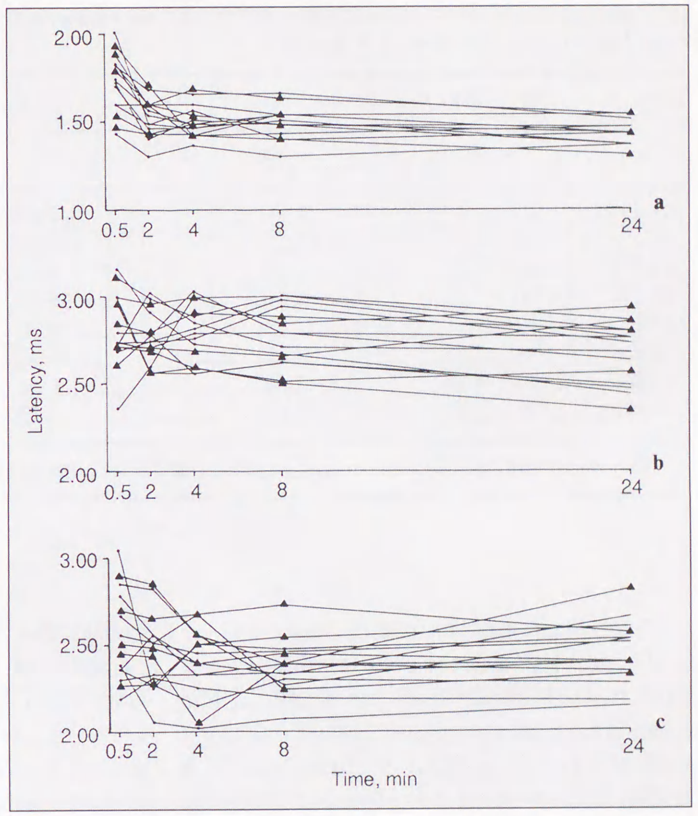

Fig. 2. Time course of peak latency of wave 1 (**a**), interpeak latencies of waves 1–3 (**b**) and 3–5 (**c**) from 0.5 to 24 h after birth for 15 neonates in whom all 5 measurements spanning 0.5–24 h after birth were possible. Ten (●) were vaginally delivered and 5 (▲) by scheduled cesarean section. Because of some overlap, the total number (● and ▲) is less than 15 for some latencies on some occasions.

Table 2. Time course of mean, decreasing rate and SD of peak latency of wave 1 representing the peripheral conduction time (peak I latency)

Time after birth	n	Peak I latencies, ms mean	p	SD	p
30 min	37	1.82		0.23	
2 h	40	1.69	< 0.05	0.26	NS
4 h	43	1.69	< 0.05	0.27	NS
8 h	40	1.65	< 0.01	0.25	NS
24 h	42	1.53	< 0.001	0.13	< 0.001
2 days	44	1.51	< 0.001	0.12	< 0.001
4 days	44	1.50	< 0.001	0.12	< 0.001
1 month	43	1.42	< 0.001	0.09	< 0.001

NS = Not significant; Student's t test (means) and Anova analysis (SD).

Table 3. Time course of mean, decreasing rate and SD of interpeak latency of waves 1–5 representing the central conduction time (peak I–V latency)

Time after birth	n	Peak I–V latencies, ms			
		mean	p	SD	p
30 min	37	5.45		0.26	
2 h	40	5.35	NS	0.28	NS
4 h	43	5.34	NS	0.39	NS
8 h	40	5.33	< 0.05	0.29	NS
24 h	42	5.25	< 0.01	0.30	NS
2 days	44	5.23	< 0.01	0.32	NS
4 days	44	5.21	< 0.01	0.31	NS
1 month	43	5.12	< 0.01	0.25	NS

NS = Not significant; Student's t test (means) and Anova analysis (SD).

Cross-Sectional Analysis of ABR

The transition of the peak latency of wave 1 is cross-sectionally analyzed in table 2. The mean latency of wave 1 decreased by 0.13 ms from 0.5 to 2 h, by 0.12 ms from 8 to 24 h and by 0.08 ms from 4 to 30 days after birth. The hourly rate of decrease was maximal (0.09 ms/h) during the period from 0.5 to 2 h after birth. A significant difference from the value recorded 0.5 h after birth in mean peak latency of wave 1 began to be noted 2 h after birth ($p < 0.05$). The minimum standard deviation was 0.23 ms for the first 8 h. Thereafter, the standard deviations decreased within a range of 0.09 and 0.13 ms. There was a significant difference in standard deviations between 0.5 and 24 h after birth ($p < 0.001$).

Table 3 shows a cross-sectional analysis of change in the interpeak latency of waves 1–5. The mean latency of waves 1–5 decreased by 0.10 ms from 0.5 to 2 h, by 0.08 ms from 8 to 24 h and by 0.09 ms from 4 to 30 days after birth. The hourly rate of decrease was highest (0.07 ms/h) during the period from 0.5 to 2 h. A significant difference from the value recorded 0.5 h after birth in mean interpeak latency first appeared 8 h later ($p < 0.05$). The maximum and minimum standard deviations during the first month were 0.39 and 0.25 ms, respectively. There was no significant difference in these standard deviations.

Table 4. Time course of mean, decreasing rate and SD of interpeak latency of waves 1–3 (peak I–III latency)

Time after birth	n	Peak I–III latencies, ms			
		mean	p	SD	p
30 min	37	2.82		0.19	
2 h	40	2.81	NS	0.23	NS
4 h	43	2.81	NS	0.23	NS
8 h	40	2.79	NS	0.20	NS
24 h	42	2.76	NS	0.19	NS
2 days	44	2.78	NS	0.20	NS
4 days	44	2.75	NS	0.17	NS
1 month	43	2.74	NS	0.15	NS

NS = Not significant; Student's t test (means) and Anova analysis (SD).

Table 5. Time course of mean, decreasing rate and SD of interpeak latency of waves 3–5 (peak III–V latency)

Time after birth	n	Peak III–V latencies, ms			
		mean	p	SD	p
30 min	37	2.63		0.27	
2 h	40	2.48	NS	0.23	NS
4 h	43	2.48	NS	0.23	NS
8 h	40	2.47	< 0.05	0.23	NS
24 h	42	2.41	< 0.001	0.23	NS
2 days	44	2.41	< 0.01	0.24	NS
4 days	44	2.42	< 0.001	0.24	NS
1 month	43	2.32	< 0.001	0.23	NS

NS = Not significant; Student's t test (means) and Anova analysis (SD).

Tables 4 and 5 summarize the results of analyses in which the interpeak latency of waves 1–5 was divided into interpeak latencies of waves 1–3 and 3–5. When mean interpeak latencies of waves 1–3 were compared to each other, the maximal decrease between two different occasions was only 0.03 ms. The maximum and minimum standard deviations were 0.23 and 0.15 ms, respectively. There was no significant difference between the mean or standard deviation of this latency recorded 0.5 h after birth and those recorded thereafter. The mean interpeak latency of waves 3–5 decreased by 0.15 ms from 0.5 to 2 h, by 0.06 ms from 8 to 24 h and by 0.10 ms from 4 to 30 days after birth. There was a significant difference between the value recorded 0.5 h after birth and those of 8 and more hours later. The hourly rate of decrease was greatest (0.10 ms/h) during the period from 0.5 to 2 h after birth. The maximum and minimum standard deviations were 0.27 and 0.23 ms, respectively, and there was no significant difference in standard deviations.

As shown above, the cross-sectional analysis of ABR disclosed a sharp decrease in the peak latency of wave 1 within 2 h after birth and lower standard deviations of the latency after 24 or more hours as compared to those of the interpeak latencies of waves 1–3 and 3–5. The decrease in the latency of waves 1–5 seemed to be due to a decrease in that of waves 3–5, in which the hourly variance was highest during the first 2 h after birth, while the interpeak latency of waves 1–3 diminished gradually.

Discussion

In studying the changes in ABR latency following a sudden change in auditory environment from inside to outside the uterus [10], we need to rule out damage to the acoustic conduction pathway caused by stress during delivery (in particular hypothermia and hypoxia). Marsch et al. [16] reported that hypothermia caused a decrease in central conduction time in animals. Therefore, we used an infant warmer in our study to prevent hypothermia immediately after birth and ruled out hypothermia by determining the rectal temperature of the neonates. Prolonged latency of each ABR wave in a case of severe anoxic encephalopathy has been reported by Hecox et al. [7]. He followed neonates with asphyxia with an electroencephalogram and ABR [7], and found that there were rarely abnormal findings in the ABR examination in the cases whose electroencephalograms were suppressed by hypoxia and hypercapnia. The brainstem is thought to tolerate hypoxic stress better than the brain cortex [17]. In the present study, neonates satisfying the following requirements were selected to exclude those with asphyxia: (1) Apgar score 8 or greater and (2) pH greater than 7.25, base excess greater than –10.0 mEq/l and P_{CO_2} less than 60 mm Hg in umbilical arterial blood. Neonates delivered by scheduled cesarean section were considered as neonates who suffered no stress (including hypoxia) during delivery. When ABR latencies were compared between these neonates and the transvaginally delivered neonates, no significant intergroup difference was observed. Goldstein et al. [13] reported a similar comparison which was made within 3 days after birth. These results allow us to rule out the influence of various stresses, including hypoxia during transvaginal delivery, on the latency of each ABR wave determined in our study.

ABR latency has been analyzed in many previous studies, dividing it into the peak latency of wave 1, reflecting the function of the peripheral acoustic pathway, and the interpeak latency of waves 1–5, representing the central conduction time (from the acoustic nerve to the inferior colliculus in the mesencephalon) [4, 6, 8, 11, 12, 18]. In our present study, besides the two latencies evaluated, the interpeak latency of waves 1–5 was subdivided into the interpeak latency of waves 1–3 and 3–5, which represents a higher level of the acoustic system.

In a longitudinal study within 24 h after birth, the interpeak latencies of waves 1–3 and 3–5 varied in many neonates, in contrast to the peak latency of wave 1 which showed a uniform decrease. Two or more days after birth, however, all these latencies decreased uniformly in measurements during sleep after lactation. Within 24 h after birth, ABR testing was performed at prescribed times irrespective of the neonate's condition (asleep or awake). Some investigators reported that the middle latency (above wave 5) in the adult human varied according to consciousness levels [19–23]. The absence of a uniform decrease in the early latency (below wave 5) in the present study may be explained by these factors. However, we cannot make a definite conclusion at present, because some investigators claim that these latencies are not affected by consciousness levels in the adult human [19, 24].

Regarding the transition of the mean peak latency of wave 1, Rubinstein and Sohmer [15] reported its decrease from 1.81 ms (2 h after birth) to 1.77 ms (8 h after birth) but found no significant change from 2 to 8 h after birth. In the present study, which employed an auditory stimulus of similar frequency [7, 12] but higher intensity [2, 25], the peak latency of wave 1 was shorter at both 2 h (1.69 ms) and 8 h after birth (1.65 ms), as compared to the values reported by Rubinstein and Sohmer [15]. Also we traced ABR starting 30 min after birth so as to more precisely study the change after birth. This analysis disclosed a significant decrease in latency during a period from 0.5 to 2 h after birth ($p < 0.05$). Because amniotic fluid remaining in the external acoustic meatus was removed immediately after birth [26] and the peripheral acoustic pathway is morphologically complete at term [27], this sharp decrease in the peak latency of wave 1 seems to represent the adaptation of the acoustic system, including the cochlear nerve (i.e. change in middle ear impedance [28] and increase in cochlear sensitivity [11, 27]) following the sudden change in auditory environment from inside to outside the uterus [10].

On the other hand, the interpeak latency of waves 1–5 central (conduction time) did not sharply decrease immediately after birth, suggesting that the influence of myelination or synaptic efficiency [11] (which are chiefly associated with central conduction time) was weak. A significant difference from the latency of waves 1–5 recorded 0.5 h after birth was first observed at 24 h ($p < 0.01$). Of the interpeak latency of waves 1–5, that of waves 3–5 changed more than that of waves 1–3. In the analysis of the standard deviations of latencies, that of wave 1 decreased significantly 24 h and later, while those of waves 1–5, 1–3 and 3–5 hardly changed. These results seem to be attributed not only to continuous improvement in myelination and synaptic efficiency in the central conduction pathway after birth as suggested by Starr et al. [11] but also to extrauterine development of the neonatal brainstem from its lower to upper level as suggested by Woods and Pressinger [26].

The present study disclosed that rapid changes with different time intervals occur in the peripheral and central acoustic functions in the human immediately after birth. However, it is impossible to perform continuous ABR monitoring in the human, starting in the fetal period. In an animal study by Woods and Pressinger [26], the changes in latencies in lambs from the intrauterine to the neonatal period were traced. The decreased rate of peak latency of wave 1 and the interpeak latency of waves 1–3 did not differ before and after birth, while that of interpeak latency of waves 3–5 was larger after birth. Although the observation was restricted to a short period, their findings are valuable in clarifying the interaction between development of the acoustic system and change in environments associated with birth.

In the future, we plan to compare neonates born at different gestational ages to explore how the postdelivery transitions in

ABR latencies vary according to differences in intrauterine environment and development stage of the acoustic pathway.

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